If we are going to live so intimately with these chemicals—eating and drinking them, taking them into the very marrow of our bones—we had better know something about their nature and their power.

Rachel Carson, *Silent Spring*, 1962

Functional Food Fights

One of the mostly hotly debated questions in nutrition today is whether—and how well—so-called functional foods are being regulated. Conventional foods become marketable as functional foods when they are supplemented with ingredients that confer health benefits beyond basic nutrition—souped-up soup, one might say. On 25 March 1999, the Center for Science in the Public Interest (CSPI), a nonprofit health advocacy group in Washington, DC, released a report titled *Functional Foods: Public Health Boon or 21st Century Quackery?* The report describes the functional foods markets in the United States, Japan, and the United Kingdom, and issues a strong call to the U.S. Food and Drug Administration (FDA) to more tightly regulate the labeling and marketing of these products.

Functional foods hold tremendous promise for benefiting public health. Problems arise, says the report, when functional foods claim that a particular ingredient confers some health benefit when there may be no conclusive evidence supporting the claim. Some functional food products may contain insignificant amounts of the promoted ingredient as well as unhealthful ingredients, such as fat and sugar, that override any health benefit provided by the functional ingredient.

Food for thought. Grocery manufacturers, the FDA, and public interest groups are embroiled in a debate over the labeling of functional foods.

A key problem, contends the report, is that the distinction between foods and drugs is becoming increasingly blurred as the number of functional foods on the market continues to grow. Some functional foods are being marketed as dietary supplements, says Ilene Ringel Heller, a senior staff attorney for the CSPI and a coauthor of the report, when they should be regulated as foods with unapproved additives or as drugs. Dietary supplements are defined under the 1994 Dietary Supplement Health and Education Act (DSHEA, pronounced "de SHAY") as edible substances with ingredients such as vitamins, minerals, herbs, and amino acids that are taken to augment the nutrients derived from conventional foods. Prior to 1994, the FDA could regulate dietary supplements as food additives, which must have FDA approval prior to marketing unless they are considered to be generally recognized as safe. DSHEA prohibited the FDA from treating dietary supplements as food additives; although the FDA still requires a 75-day notification period prior to the marketing of a new dietary supplement (during which time the agency may challenge any labeling claims made by the manufacturer), FDA approval is not actually required for a dietary supplement to be put on the market.

DSHEA also allows the use of structure/function claims on supplement labels. These statements can be difficult to distinguish from health claims—claims that a product will prevent, cure, or treat a disease—which must be specifically approved by the FDA. For example, the structure/function claim "Calcium is necessary for bone growth and development" becomes a health claim if the word "osteoporosis" is introduced into the statement.

The CSPI report claims that some manufacturers seek to avoid costly and time-consuming FDA approval entanglements by taking advantage of what it classifies as DSHEA's less stringent provisions; indeed, says Heller, some manufacturers are marketing functional foods as dietary supplements and making structure/function claims that are essentially implied health claims. For instance, says the report, the labels on Hain Kitchen Prescription canned soups, which contain medicinal herbs such as echinacea, indicate the products are supplements and feature structure/function claims normally found on dietary supplement labels. But Stacey Zawel, vice president of scientific and regulatory policy at Grocery Manufacturers of America, an industry organization based in Washington, DC, says this is an inaccurate leap on the report's part. She says, "Provisions for functional foods and dietary supplements are simply different—not necessarily less or more stringent. If you really dissect the laws, you will find that it's a wash as to which is more difficult. . . . The law already requires all products to present labeling information that is truthful and not misleading. There is no difference for any claim you make on your food, structure/function or otherwise." Furthermore, Zawel says, there is absolutely no evidence of an onslaught of inappropriate structure/function claims. She says, "Every example that is provided in [the CSPI report] is perfectly legal under FDA law." Heller calls this stance "disingenuous," saying, "The examples . . . speak for themselves."

The report makes several recommendations for FDA action. First, the FDA should prohibit companies from marketing functional foods as dietary supplements, and make it clear that health claims for functional foods are subject to the same preapproval requirements that apply to all other foods. Functional ingredients added to foods should be regulated as food additives unless they are generally recognized as safe, and the FDA should also impose tighter regulation of structure/function claims for foods and require that they be based on universally recognized scientific facts, such as the fact that calcium is necessary for bone growth and development. The report also recommends that the FDA establish a postmarket surveillance system that would monitor adverse health effects from functional ingredients in foods. Finally, the report recommends that the FDA require foods making structure/function claims to meet certain nutritional guidelines: they must not contain unhealthful levels of fat, saturated fat, cholesterol, or sodium, and they should, prior to fortification, contain at least 10% of the recommended daily intake of certain desirable nutrients such as vitamin C.

For now, the two sides of the functional foods debate remain at loggerheads. Zawel says, "[Functional foods] are governed by all laws covering conventional foods. It is that simple. The FDA has conveyed to us that, in fact, no new regulations are needed to regulate these products." Heller maintains, however, that "the FDA has to begin

addressing the regulation of functional foods. 'Functional foods' is a concept that everyone knows about but for which there is no official policy. The FDA must face the issues raised by these products to ensure that functional foods become a public health boon rather than the snake oil of the 21st century."

Estrogen's a Natural in Herbal Remedies

Patricia Eagon, an associate professor of medicine at Pennsylvania's University of Pittsburgh, decided to consult an herbalist after she began to suspect that Premarin, the prescription estrogen she was taking for menopausal symptoms, was causing a rash on her leg. The herbalist, whom she had consulted before on other health matters, gave her a mixture of several herbs to take instead of Premarin. The concoction both relieved Eagon's hot flashes and piqued her curiosity about how the herbal ingredients worked.

Eagon decided to launch her own experiment to find out. She conducted an estrogen-binding assay on 15 herbs commonly used in treating menopause, including 3 from the remedy she had taken herself. Herbs that showed estrogenic activity in the screening were then fed to rats that had undergone ovariectomy. To test the herbs' estrogenicity, Eagon weighed the rats' uteri at the end of the study and measured changes in the concentration of luteinizing hormone in their blood (enlarged uterus and decreased luteinizing hormone concentration are both indicators of estrogenic activity). The tests indicated an estrogenic effect in four of the herbs—chaste tree berry (*Vitex agnus-castus*), dong quai (*Angelica sinensis*), American ginseng (*Panax quinquefolium*), and black cohosh (*Cimicifuga racemosa*). Eagon reported her findings on 11 April 1999 at the annual meeting of the American Association for Cancer Research and is currently preparing the results for publication.

Eagon's findings have implications for the fast-growing number of people who are embracing alternative medicine. According to the U.S. Food and Drug Administration (FDA), more than half of all U.S. adults use over-the-counter vitamins, dietary supplements, or herbal remedies. Ann Fonfa, founder of the New York City–based Annie Appleseed Project to promote the study of alternative cancer treatments, estimates (based on national averages for the general population) that 30% of menopausal women treat themselves with medicinal herbs, many because they believe such herbs are safer and gentler than prescription drugs. Yet they have no proof of the herbs' medicinal value and safety beyond the folk wisdom of herbalists; unlike pharmaceutical manufacturers, manufacturers of herbal remedies are not required by the FDA to prove their products' safety and efficacy.

Eagon's discovery of estrogenicity in the herbs she tested comes as no surprise to some researchers. "While the specific findings are new, there is well-known, well-described estrogenic activity in plants," says Daniel Sheehan, director of the Endocrine Disruptor Knowledge Base Program of the FDA's National Center for Toxicology Research in Jefferson, Arkansas. He points to the example of subterranean clover, a type of clover that farmers have known for 50 years to cause reproductive failure in sheep.

While Eagon's research may help explain why certain herbs may relieve hot flashes and other menopausal symptoms, it raises several more questions. Of key interest is how these phytoestrogens react in the body. "We really need to measure these things in women," Eagon says.

Laura J. Stafford

Herbal estrogens. A recent study by associate professor of medicine Patricia Eagon suggests that some herbs may have powerful estrogenic properties.

Premarin has long been doctors' drug of choice in treating menopause because it not only relieves symptoms but also helps prevent osteoporosis and heart disease. However, the synthetic hormone also elevates women's risk of breast and uterine cancer, which scares many would-be users away.

Because of the estrogenic activity she observed in the herbs she studied, Eagon feels compelled to warn women at high risk of breast or uterine cancer against taking them, as estrogen has been implicated in some forms of cancer. Yet she admits she doesn't know if the herbs promote cancer. In fact, she says, "We may test these further and find they inhibit cancer. It looks as if soy has a positive effect in preventing breast cancer. These herbs may also be able to prevent it."

Eagon also doesn't know if estrogenic herbs give women the same protection against heart disease and osteoporosis that synthetic estrogen does. "One question is, how do estrogenic substances from plants compare in activity with pharmaceutical estrogens," says Fredi Kronenberg, director of the Rosenthal Center for Complementary and Alternative Medicine at Columbia University College of Physicians and Surgeons in New York City. "Do they have a broad spectrum of estrogenic activity or are they more selective in action? We don't have the answer yet."

Some of those answers may come out of Eagon's upcoming research. She first plans to investigate whether the herbs inhibit or promote breast cancer by feeding them to rats with a genetic susceptibility to the disease. Eagon also plans to delve into the herbs' effects on premenopausal women. Younger women take chaste tree berry and dong quai for premenstrual syndrome, amenorrhea, and infertility; American ginseng is recommended for stomach upset, lack of appetite, physical exhaustion, and infection. Eagon would use mice with intact ovaries to simulate the impact on premenopausal women.

"People think [taking herbal remedies] is like eating another serving of broccoli," Eagon says. "These things are not all benign. The more we know about them, the better off we'll be."

Harvesting Monoclonal Antibodies from Plants

When monoclonal antibodies were first developed 20 years ago, they were hyped as a magic bullet for curing cancer and other diseases. However, killing cancer cells with these immune proteins, which are artificially produced and which neutralize one specific antigen or foreign protein, was not as straightforward as first assumed, and clinical failures occurred. Moreover, the high cost of producing monoclonal antibodies by traditional cell fermentation methods limited their applications. These setbacks have forced scientists to look more realistically at monoclonal antibodies.

Now, researchers at EPIcyte Pharmaceutical, based in San Diego, California, hope to revitalize interest in monoclonal antibodies with a new technology that produces large supplies of the proteins inexpensively. Their new technology uses green